From the
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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)	
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2004/051578	22.07.2004	23.07.2003

International Patent Classification (IPC) or both national classification and IPC
A61K31/4439, A61P1/04

Applicant
ALTANA PHARMA AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Collura, A Telephone No. +49 89 2399-7870

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was field, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The following document has not been furnished:

   ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 12 (with respect to IA)

because:

☒ the said international application, or the said claims Nos. 12 (with respect to IA) relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	
	No:	Claims	1-12
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-12
Industrial applicability (IA)	Yes:	Claims	1-11
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III.

Claim 12 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V.

The following documents (D) are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

D1: US-B1-6 410 569 (KOHL BERNHARD) 25 June 2002 (2002-06-25)
D2: US-A-5 693 818 (VON UNGE SVERKER) 2 December 1997 (1997-12-02)

For what concerns the most important passages of the above-mentioned documents, please see citations in the International Search Report, unless otherwise stated.

NOVELTY AND INVENTIVE STEP

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-12 is not new in the sense of Article 33(2) PCT.

a) Document D1 discloses pantoprazole magnesium dihydrate, its use for the manufacture of a medicament for the treatment of gastrointestinal diseases and the method for preparing said compound.
Said method consists of (a) adding a solution of $MgCl_2$ hexahydrate to a solution of pantoprazole Na sesquihydrate and (b) precipitating the solid compound.
D1 also teaches that the dihydrate of the magnesium salt of pantoprazole has surprising stability properties.
The subject-matter of claims 1-12, therefore, seems to be already anticipated by D1.

b) Document D2 describes the use of single enantiomers of omeprazole magnesium salt for the manufacture of a pharmaceutical formulation suitable for the treatment of gastrointestinal problems.

According to what is disclosed in the description (col. 4, lines 11-34), the method for obtaining the claimed compounds comprises the following steps:

(i) separation of the two stereoisomers of a diastereoisomeric mixture of formula IV, in order to obtain the two enantiomers of omeprazole;

(ii) treatment of each single enantiomer obtained with NaOH in aqueous or non-aqueous medium;

(iii) treatment of the optically pure Na+ salts of omeprazole with $MgCl_2$ in aqueous solution.

Said method corresponds to the one used for preparing the compounds according to the present invention.

It is, therefore, not clear how, according to the present application, it would be possible to obtain alkaline salts which are different from those obtained according to the method described in D2.

Claims 1-4, 11 and 12 are, therefore, considered to not novel.

Claims 4-10 are referred to the magnesium salts of pantoprazole. Although D2 refers to the preparation of the magnesium salts of omeprazole, it would be obvious for the skilled person to apply such method to any compound with the falling into the same class of structures.

Thus, the subject-matter of claims 5-10 is not considered as involving an inventive step.

INDUSTRIAL APPLICABILITY

For the assessment of the present claim 12 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.